

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 August 2005 (04.08.2005)

PCT

(10) International Publication Number  
**WO 2005/070957 A1**

(51) International Patent Classification<sup>7</sup>: **C07K 14/00**,  
14/02, C07H 21/00, 21/04, C12Q 1/00, 1/70, C12N 9/00

(21) International Application Number:  
**PCT/US2005/000292**

(22) International Filing Date: 6 January 2005 (06.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/535,708 9 January 2004 (09.01.2004) US

(71) Applicant (for all designated States except US): **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GRAHAM, Donald,**

J. [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **SIMCOE, Amy, L.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **LUDMERER, Steven, W.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **FLORES, Osvaldo, A.** [CL/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **LAFEMINA, Robert, L.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(74) Common Representative: **MERCK & CO., INC.**; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,

*[Continued on next page]*

(54) Title: HCV RNA-DEPENDENT RNA POLYMERASE

(57) Abstract: The present invention features NS5B polypeptides from different clinically important HCV genotypes. The polypeptides can be used individually, or as part of a panel of RNA-dependent RNA polymerases, to evaluate the effectiveness of a compound to inhibit NS5B activity.

MSMSYTWTGALITPCPSEEKLPISPLNSLIRHENRYATTYTSRASVTRQKVVTFDRQLVLDQHVKTAKEVKEA  
RASKVAKRLTTEACDLPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
FASRVKARNTTPEACLVPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
DPFKGGRKPARLYVPPDLGVVQCEKRALYDVQKLGSIEITGSAYGFQYSPCCVERELKKMPSKXTP\_GFSYET  
RCFDSTVTEKJLVEEEVYQCCDLEPZARKVJTAALTERLYVSGFMHNSKGDLCGYRNCRASGVY\_TTSFGNTLTC  
YIKAAQACRAAGIJDPMVMLVCGDOLVVIESCGQEDSERNUKAPTEAMTYSAPPGDPRPEYDLELLITSCSSN  
VSVAADDNGKGRYYYL73DTTPPLARANMETARPKPVSNSLGNILMIAFTIWWRMWMTHTFSIIOSQEILDRLPL  
DFDMYGATYSVTPLJMPA113RLIUGLSAFTL11SYSPVS11RVRAGTLRNLGLCPPLRAWJHRA3AVRAKU\_IAQGGK  
AKICGGYLYENWAVRXTTNTPLPATQQLDLSWSWTTVGAGGGDIYHSNSRKR

A

MSMSYTWTGALITPCPSEEKLPISPLNSLIRHENRYATTYTSRASVTRQKVVTFDRQLVLDQHVKTAKEVKEA  
RASKVAKRLTTEACDLPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
FASRVKARNTTPEACLVPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
DPFKGGRKPARLYVPPDLGVVQCEKRALYDVQKLGSIEITGSAYGFQYSPCCVERELKKMPSKXTP\_GFSYET  
RCFDSTVTEKJLVEEEVYQCCDLEPZARKVJTAALTERLYVSGFMHNSKGDLCGYRNCRASGVY\_TTSFGNTLTC  
YIKAAQACRAAGIJDPMVMLVCGDOLVVIESCGQEDSERNUKAPTEAMTYSAPPGDPRPEYDLELLITSCSSN  
VSVAADDNGKGRYYYL73DTTPPLARANMETARPKPVSNSLGNILMIAFTIWWRMWMTHTFSIIOSQEILDRLPL  
DFDMYGATYSVTPLJMPA113RLIUGLSAFTL11SYSPVS11RVRAGTLRNLGLCPPLRAWJHRA3AVRAKU\_IAQGGK  
AKICGGYLYENWAVRXTTNTPLPATQQLDLSWSWTTVGAGGGDIYHSNSRKR

B

MSMSYTWTGALITPCPSEEKLPISPLNSLIRHENRYATTYTSRASVTRQKVVTFDRQLVLDQHVKTAKEVKEA  
RASKVAKRLTTEACDLPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
FASRVKARNTTPEACLVPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
DPFKGGRKPARLYVPPDLGVVQCEKRALYDVQKLGSIEITGSAYGFQYSPCCVERELKKMPSKXTP\_GFSYET  
RCFDSTVTEKJLVEEEVYQCCDLEPZARKVJTAALTERLYVSGFMHNSKGDLCGYRNCRASGVY\_TTSFGNTLTC  
YIKAAQACRAAGIJDPMVMLVCGDOLVVIESCGQEDSERNUKAPTEAMTYSAPPGDPRPEYDLELLITSCSSN  
VSVAADDNGKGRYYYL73DTTPPLARANMETARPKPVSNSLGNILMIAFTIWWRMWMTHTFSIIOSQEILDRLPL  
DFDMYGATYSVTPLJMPA113RLIUGLSAFTL11SYSPVS11RVRAGTLRNLGLCPPLRAWJHRA3AVRAKU\_IAQGGK  
AKICGGYLYENWAVRXTTNTPLPATQQLDLSWSWTTVGAGGGDIYHSNSRKR

C

MSMSYTWTGALITPCPSEEKLPISPLNSLIRHENRYATTYTSRASVTRQKVVTFDRQLVLDQHVKTAKEVKEA  
RASKVAKRLTTEACDLPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
FASRVKARNTTPEACLVPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
DPFKGGRKPARLYVPPDLGVVQCEKRALYDVQKLGSIEITGSAYGFQYSPCCVERELKKMPSKXTP\_GFSYET  
RCFDSTVTEKJLVEEEVYQCCDLEPZARKVJTAALTERLYVSGFMHNSKGDLCGYRNCRASGVY\_TTSFGNTLTC  
YIKAAQACRAAGIJDPMVMLVCGDOLVVIESCGQEDSERNUKAPTEAMTYSAPPGDPRPEYDLELLITSCSSN  
VSVAADDNGKGRYYYL73DTTPPLARANMETARPKPVSNSLGNILMIAFTIWWRMWMTHTFSIIOSQEILDRLPL  
DFDMYGATYSVTPLJMPA113RLIUGLSAFTL11SYSPVS11RVRAGTLRNLGLCPPLRAWJHRA3AVRAKU\_IAQGGK  
AKICGGYLYENWAVRXTTNTPLPATQQLDLSWSWTTVGAGGGDIYHSNSRKR

D

MSMSYTWTGALITPCPSEEKLPISPLNSLIRHENRYATTYTSRASVTRQKVVTFDRQLVLDQHVKTAKEVKEA  
RASKVAKRLTTEACDLPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
FASRVKARNTTPEACLVPPHSARSKFGYQAKDVASHSRKAHEITSSVVKDLLCDDNTTIPPTIMAKNEVFCV  
DPFKGGRKPARLYVPPDLGVVQCEKRALYDVQKLGSIEITGSAYGFQYSPCCVERELKKMPSKXTP\_GFSYET  
RCFDSTVTEKJLVEEEVYQCCDLEPZARKVJTAALTERLYVSGFMHNSKGDLCGYRNCRASGVY\_TTSFGNTLTC  
YIKAAQACRAAGIJDPMVMLVCGDOLVVIESCGQEDSERNUKAPTEAMTYSAPPGDPRPEYDLELLITSCSSN  
VSVAADDNGKGRYYYL73DTTPPLARANMETARPKPVSNSLGNILMIAFTIWWRMWMTHTFSIIOSQEILDRLPL  
DFDMYGATYSVTPLJMPA113RLIUGLSAFTL11SYSPVS11RVRAGTLRNLGLCPPLRAWJHRA3AVRAKU\_IAQGGK  
AKICGGYLYENWAVRXTTNTPLPATQQLDLSWSWTTVGAGGGDIYHSNSRKR

E

WO 2005/070957 A1



MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,

SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*